MHRA experience with CIDs and recommendations derived from it

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MHRA continues to support novel trials
Clinical Trial Transformation Initiative (CTTI)

- Regulators (FDA, MHRA), academia, industry, consultants developed a guide to Master Protocol trials
- Set of tools to guide appropriate use of master protocols
- Launched: 13th of October 2020
- Pre-planning tools, as well as planning and implementation, study simulation tool and protocol development map

https://www.ctti-clinicaltrials.org/projects/master-protocol-studies
MHRA implementation plan for novel trials as part of LSIS

• Key outcome: Strengthened UK environment for clinical research that provides support for innovative trial design

• Included
  • Engagement with stakeholders on novel trials and our advice services
  • Workshop – October 2020
  • Internal training
  • Report
MHRA CTU has been tracking these trials since January 2018.

COVID-19 saw a rise in submissions – supported by NIHR and Chief Medical Officer

• Recovery
• Principle
• REMAP-CAP
• Others…..
Metrics

Trial types

- Basket
- Umbrella
- Platform
- Seamless
- TWIC
- Other

Indication

- Oncology
- Non-oncology
Recommendations
The biggest barrier to innovation and research from our perspective is not coming to ask our advice early enough (or at all!)

- Scientific advice
- Broader scope meetings
- Regulatory advice
- Innovation office meetings

Novel trial designs must, like all trials, be safe and scientifically sound. Specific guidance is available, but it is just that – guidance. It is not included in legislative requirements. Each trial is reviewed on a case-by-case basis.
### Key elements to consider – CTFG recommendation paper

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<tr>
<th><strong>Recommendation</strong></th>
<th><strong>Further consideration</strong></th>
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<tr>
<td>Clearly describe and justify the design</td>
<td>Some national competent authorities (NCAs) (not the MHRA) do not accept that First-in-human IMPs and Advanced Therapy Medicinal Products (ATMPs) are introduced via substantial amendments; some NCAs (not the MHRA) do not support trials with several independent arms and prefer they are submitted as separate trials.</td>
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<td>Maintain scientific integrity</td>
<td>The scientific hypothesis and primary objectives defined at the time of the initial CTA application should not be changed during the conduct of the trial.</td>
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<td>Ensure quality of trial conduct and optimise clinical feasibility</td>
<td>Investigator and Sponsor oversight</td>
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<td>Ensure safety of trial subjects</td>
<td>Independent Data Monitoring Committee (IDMC), communication plan</td>
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<td>Maintain data integrity</td>
<td>Type 1 error rate, confidentiality of interim results versus transparency</td>
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<td>Reassess benefit-risk balance at critical steps</td>
<td>Throughout a clinical trial: in case of safety signals, at the time of substantial amendments, consider changes of informed consent form (ICF)</td>
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<td>Validate companion diagnostics</td>
<td>In vitro diagnostic medical devices (IVDs)</td>
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<td>Consider data transparency</td>
<td>Publication policy, some NCAs require submission of data within one year (six months for paediatric trials) following the end of a sub-protocol (not absolute requirement for MHRA)</td>
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Innovative Licensing and Access Pathway

- **Goal**: to deliver efficient and timely development of medicines and earlier patient access

- A new medicine designation links to the development of a roadmap to patient access – **Innovation Passport**

- **Target Development Profile** (TDP) creates a unique UK roadmap, utilising tools from a toolkit and providing a platform for sustained multi-stakeholder collaboration

- The regulatory toolkit is intended to drive efficiencies in the development programme, supporting data generation and evidence requirements

- An integrated pathway will pull together expertise from across the MHRA and partners in the wider healthcare system including NICE and the SMC

- Built-in flexibility, with multiple entry points along the pathway (non-clinical data → clinical trials)
Some of the tools being developed in the Toolkit

- Adaptive inspections
- ATMP Centre accreditation*
- Novel CT methodology & design support
- Common medicine & device trial design
- Coordinated approvals process for co-developed medicines & IVDs
- CPRD assisted recruitment in clinical trials
- Rapid Clinical Trial Dossier pre-assessment service
- Certifications

- CPRD control groups
- Enhanced patient engagement
- Continuous benefit-risk assessments that integrate real-world evidence
- New licensing procedures:
  - Rolling review
  - Accelerated timetables for marketing authorisation, flexibilities
  - International options
    - FDA Orbis
    - ACCESS

*contact GCP.inspectorate@mhra.gov.uk
Summary

Integrated approach to support innovation in design through continued engagement with industry, charities, patients and research bodies such as the ECMC.

Develop components of a regulatory toolkit composed of required components (tools that ensure regulatory compliance) as well as those that can be selected individually to support a bespoke development programme that reflects a lifecycle approach to evidence generation.
Questions?
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